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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/849,525	08/29/1997	GHITA LANZENDORFER	435-WCG	3976

27384 7590 02/09/2006

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/849,525	LANZENDORFER ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/24/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 24, 2005 has been entered.

Claims 19-24 are pending.

Double Patenting

2. Claims 19-24 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,952,373, claims 1-5 of US Patent 6,121,243 and claims 1-2 of US patent 6,562,794. Per Applicant's request in the Amendment, filed on May 10, 2005, the double patenting rejections is held in abeyance until allowable subject matter is indicated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 19-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for applying the flavonoid containing compostion topically for treating a immunosuppressive condition caused by UV radiation, does not reasonably provide enablement for methods of preventing such immunosuppression of

skin cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:
The invention provides for methods of applying flavanoids topically to treat or prevent an immunosuppressive condition.

(2) The state of the prior art
The state of prior art does not teach methods of preventing immunosuupression of skin cells induced by UVB radiation.

(3) The relative skill of those in the art
The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art
The unpredictability of the preventative measurements is very high. The true fact that skin tissue may be protected by flavonoids does not amount to establishing any degree of prevention of a skin condition. Thus, there is not predictability in the art with respect to preventative measurements.

(5) The breadth of the claims

The claims are very broad. The claims are directed to methods of preventing any degree of immunosuppression of skin cells caused by UVB radiation.

(6) The amount of direction or guidance presented

The specification fails to provide any objective measurement of any degree of prevention of immunosuppression caused by UVB radiation. In the instant case, the burden of enabling for preventing immunosuppression of skin tissue caused by UVB radiation requires appropriate screening testing, subsequent data compilation, and finally appropriate data analysis, to assess and properly enable one skill in the art whether the claimed compositions prevent the immunosuppression of skin tissue caused by UVB radiation. For example, the specification must provide adequate guidance whether such immunosuppression can be prevented in a patient once the composition is administered to a subject susceptible to develop said immunosupression. The specification provides no guidance, in the way written description, of such measurements or analysis.

Moreover, the specification must provide direct evidence associating the claimed prevention to the composition applied. The burden of showing preventative properties is greater than that of enabling a treatment, because one of ordinary skill in the art must not only show competent screening of those subjects susceptible to such conditions, but also show that the efficacy of a preventative method is directly caused by applying or administering the instantly claimed composition to the susceptible subjects.

(7) The presence or absence of working examples

As stated above, the specification does not provide any working example as to the methods of preventing immunosuppression of skin cells induced by UVB radiation.

(8) The quantity of experimentation necessary

There are no teachings for screening methods identifying susceptible subjects nor is there any direct evidence of efficacy establishing a preventative property associated with the claimed composition. Furthermore, the state of the prior art concerning methods of preventing skin damage is not well described, nor does it provide for any absolute degree of prevention. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al US Patent 5,145,781 in view of Middleton et al (Middleton) (Middleton and Chithan,*The Flavonoids, Advances in Research Since 1986*, 1994, Chapman & Hill, London, Ch. 15, pp 619-645, already on record), Harrrison's (*Harrison's Principles of Internal Medicine*, 1994, New York, McGraw-Hill, Inc., 13th edition, pp. 309-313, already on record).

The scope of the instant claims are directed to methods of treating or prophylactically treating skin cell immunosuppression comprising flavonoids such as alpha glucosyl rutin, glucosyl rutin, optionally one or more cinnamic acid derivatives and optionally an antioxidant. The instant immunosuppression encompasses any type of biological effects that cause attenuation of immune system. Since the claims are directed to preventing immunosuppression of skin, Examiner takes the position that any patient receiving α-glycosyl rutin, even as sun screening agent, can fall within the scope of such patients in need of prophylactic treatment of immunosuppression of skin cells induced by UVB radiation.

Applicant is informed that during patent examination, the pending claims are given the broadest reasonable interpretation consistent with the specification. Accordingly, the recitation of "optionally" does not limit the instant formulations to the recited optional component.

Suzuki et al disclose α-glycosyl rutin which is a flavonoid encompassed by the instant claims. Suzuki discloses various uses of α-glycosyl rutin (col 8, lines 45-56; col 10, lines 4-30). Suzuki discloses cosmetic compositions comprising α-glycosyl rutin in amounts of about 1-10 W/V %(see col 5, lines 55-59; col 19-20, col 20, lines 30-41). Suzuki specifically discloses the use of such rutin as UV absorbant. (col 8, lines 45-55, col 22, lines 45-67). Suzuki teaches the use of his compositions for immune conditions such as malignant tumors. Suzuki also teaches the incorporation of antioxidants. (see col 21, lines 1-25). Suzuki teaches use of α-glycosyl rutin on patients as UV-absorbant, therefore, such populations are viewed to be in need of prophylactic treatment of immunosuppresion of skin cells induced by UVB radiation. Suzuki meets all elements of the instant claims except that it fails to explicitly describe the use of α-glycosyl rutin use for immunosuppression of skin cells induced by UVB radiation.

Middleton is merely used to show the plethora of information about the effects of flavonoids on immune system (pp 619-620). Accordingly, it is well within purview of an ordinary skill to modulate the activity of immune system by administering flavonoids of interest (Ch. 15, pp 619-645). For example, genistein have been shown to inhibit T-lymphocyte activity by inhibiting protein tyrosine kinase (see pp 625, 2nd col, 1st paragraph). Quercetin has been effective in regressing the spread of fibrosarcoma in

vitro (see pp 627, 2nd col). Similarly, flavonal glycosides such as mauritanin and myricitrin have been shown to improve the delayed-type hypersensitivity among mice undergoing two-stage carcinogenesis (see top of pp 628). Therefore, using flavanoids to improve immunosuppressive behavior of cells are well described in the art.

Moreover, like alpha glucosyl rutin, topical quercetin has been effective in preventing and improving various immunosuppressive conditions associated with skin cancer (see pp 642, 3rd -8th paragraphs). Therefore, the general knowledge available in the art provides for the beneficial effects of topical flavonoids in improving immunosupresseive conditions regardless of their etiology.

Harisson's is used to show the general knowledge in the art about the etiology of solar radiation and systemic immune response caused by UV-B exposure (see pp 309 last paragraph). Accordingly, the immunosuppression caused by UV-B is caused by the induction of suppressor T cells throughout the body.

Middleton and Harisson's collectively teach the general knowledge of an ordinary skill in the art of medicine and immunology about the beneficial effects of flavonoids on immune system; and the etiology of immunosuprression cause by UV-B.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to apply Suzuki's formulations topically and either treat or prophylactically treat patients in need of reversing the immune suppressions caused by UV-B exposure, because as taught Harrison's, such immunosuprression is dependent on the activity of T-lymphocyte which as taught by Middleton, can be controlled by topical administration of a flavonoid of choice.

Thus, one of ordinary skill in the art understanding the etiology of UV-B induced skin conditions would have had a reasonable expectation of success in applying Suzuki's formulations for its immunologic effects because as taught by Middleton, the ordinary skill in the art would have had a reasonable expectation of success for its beneficial immune effects.

Moreover, the instant method claims 19 and 25 are not limited to any specific etiology associated with UV-B induced immunesuppression; rather, said claims are limited to the recitation of a single method steps, wherein the method comprise applying to the skin of a person an effective amount of one or more flavonoids. Accordingly, the instant claims are *prima facia* obvious over the cited prior art, because the ordinary skill in the art would have known of various beneficial effects of flavonoids on immune system at least as a prophylactic treatment when using Suzuki's compositions topically as a sunscreen or UV absorbant.

Response to Arguments

5. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the references does not explicitly treat methods for treating immunosuprression of skin cells induced by UVB radiation. (see arguments at page 8).

In response Examiner states that had Suzuki explicitly described such limitation, it would have been used as an anticipatory prior art under 35 USC § 102. Here, contrary to Applicant's position, Suzuki clearly teaches cosmetically or dermatologically effective amounts of α-glycosyl rutin at numerous places for topical administeration (see col 17-col 20). The secondary references are used to establish that any person in need of

using a sunscreen or UV absorbent, is inherently in need of prophylactic treatment of any immunosupression of skin tissue induced by UVB radiation. Accordingly, the combined teachings of references meet all elements of the instant claims.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

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